18. (Amended) A method according to Claim 16 wherein said cell-line is a high-secretor variant which when exposed to a pre-selected substance results in at least 25-45% mediator release.

REMARKS

Reconsideration and withdrawal of the rejection with respect to claims 16-24 are respectfully requested in view of the foregoing amendments and the following remarks.

Considering initially the objections to the drawings, the same will be attended to upon allowance of the claims.

With respect to the oath or the declaration as being defective in that non-initialed and/or non-dated alterations have been made to the address of inventor Helm, enclosed herewith is a photocopy of the corrected declaration which was recently submitted in connection with the parent application.

With respect to the § 112 rejection of claim 19 as set forth in paragraph 19, enclosed herewith is a copy of a Certificate from the ECACC at Porton Down certifying that the cell-line RBL-2H3 H2/2/C has an accession number of 93112513 and has been deposited in accordance with The Budapest Treaty 1977; please note that the deposit number is also the accession number. The specification has been amended at page 2, line 6 to identify this deposit and a Declaration Under 37 C.F.R. § 1.808 is also enclosed.

With respect to the § 112 rejection of claim 17 as set forth in paragraph 20, the phrase "sensitizing agent" has been changed to "human IgE" to resolve this objection. With respect to the 112 rejection of claim 16-24 as being indefinite for the reasons set forth in paragraph 21, claim 16 and 17 have been amended to replace the phrase "sensitizing agent" with "human IgE"; in addition, in claim 17 the phrase "secretor variant" has also been deleted. With respect to claims 18 and 19 and the term "secretor variant", although the term "secretor variant" has no art recognized equivalent, the same is extensively defined with supporting experimental data in the above application. Moreover, the aforementioned deposit of the high secretor variant provides enablement to those wishing to repeat and confirm the characteristics of the high secretor variant; please see page 2, line 17 to 31; Figure 1 showing the release of 5-hydroxytryptamine (5HT) from transfected cell-lines; page 12, line 10 to 14 indicating the secretion characteristics of a low secretor variant as compared to a high secretor variant; and Table 1 which directly compared RBL-2H3 intermediate secretors with high secretors. In addition, Claim 18 has been amended to provide further definition of this phrase - namely a high secretor variant which then exposed to a pre-selected substance results in at least 25-45% mediator

release (specific support for which can be found in the specification at pg. 12).

Regarding the priority issues set forth in paragraph 22, it should be noted that claim 20 has been limited to a "radioactive" marker and claim 24 has been limited to a "radio-immunoassay".

With respect to the rejection of claim 17 as being unpatentable over Wilson et al., it should be noted that this manuscript was published in the summer of 1993 and the present application has a claimed priority date of November 28, 1992. Accordingly, it is believed that the Wilson et al. reference is not an appropriate reference against the application.

Concerning finally the '103 rejection of claim 16-24 as being unpatentable over Cantor et al. in view of Gilfillan et al. and Levi-Schaffer et al., the Examiner states that Cantor et al. teaches methods for determining the allergic status of an individual. The claims of the above application (claims 16 and 17 and the dependent claims thereof) relate to a method for determining the potential irritancy or allergenicity of a pre-selected substance. The above application therefore relates to a quite separate type of diagnostic system, that of testing the potential of substances to promote an allergic response rather than determining the allergic status of an individual. The former

relates to the identification of substances that may predispose an individual to an allergic response. The latter relates to a method to identify individuals that are already sensitized to selected substances.

Applicants do not dispute that Gilfillan et al. teaches that RBL-2H3 cell-lines transfected with the α-chain of the human FcεR1 can be sensitized by exposure to human IgE and that the human FcεR1α can interact with the β and γFcεR1 subunits to elicit a secretory response from mast cells.

The RBL-2H3 cell line described in Gilfillan et al. is exposed to a well-characterized IgE (anti-TNP IgE) and is sensitized to a well characterized antigen (TNP conjugated to ovalbumen). This does not relate to the use of the cell line of the invention to determine the potential irritancy or allergenicity of pre-selected substances.

The Examiner has combined the disclosures in Cantor et al. with that of Gilfillan et al. to render the above application as obvious. This conclusion is respectfully traversed since in both citations the conclusions are drawn to a cell line that has had prior exposure to the allergic substance before addition of IgE. The above application relates to the use of "virgin" substances the allergenicity of which is not known and does not require the addition of IgE.

The Examiner considers that Levi-Schaffer et al. teaches that mast cell activation results in the release of pro-inflammatory molecules which may result from an IgE independent activation. There is no disclosure in Levi-Schaffer et al. that the IgE independent activation is mediated via FcεR1 receptor. Indeed Levi-Schaffer et al. does not disclose or suggest on the mechanism via which the IgE independent pathway works. There is no link between Cantor et al., Gilfillan et al. and Levi-Schaffer et al. which would allow a person skilled in the art to conclude that the high affinity receptor mediates the IgE independent pathway.

It is respectfully submitted that it is only through hindsight reasoning can such a distorted reconstruction of the teachings of Cantor et al., Gilfillan et al., and Levi-Schaffer et al. be made and this is, of course, patently improper.

In summary, it is respectfully submitted that the disclosures in Cantor et al., Gilfillan et al. and Levi-Schaffer et al. did not render the above application obvious. It is apparent that Cantor et al. and Gilfillan et al., relate to determining which substance an individual is allergic to. The present application relates to pre-determining the likely response of an individual to a selected substance. Levi-Schaffer et al. merely discloses that mast cells may be sensitized via IgE-dependent or IgE-independent pathways. There is no teaching in any of these

references that the high affinity receptor FcεR1 is involved in the IgE-independent pathway.

In view of the foregoing, it is respectfully submitted that the claims as now amended are patentably distinguished over the references of record. Accordingly, allowance of the claims at an early date is earnestly solicited.

Respectfully submitted,

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Enclosures: Copy of Declaration
Accession form
Statement Pursuant to 37 C.F.R. § 1.808